INTERNATIONAL JOURNAL OF SCIENCE AND NATURE
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Case Study

CLINICAL DILEMMA IN A CASE OF BACTERIAL MENINGITIS WITH FALCIPARUM MALARIA

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ABSTRACT
In endemic areas, co-infection of malaria and other bacterial and/or viral infection may present with a clinical dilemma in the diagnosis and so also in the treatment approach in such cases(s).We report a 7 year old boy who initially presented with pyogenic meningitis responded to standard antibiotics as per his CSF report but continued to have high spikes of fever. While malaria microscopy and RDT repeatedly failed to diagnose malaria. On 13th day of his hospital admission he was tested positive for Falciparum Malaria by Rapid Diagnostic Kit and responded to Artesunate Combination Therapy**.** In a clinical situation where multiple infections coexist it may be advisable to do PCR for early antigen detection instead of relying on peripheral blood smear or RDT.

KEYWORDS: Bacterial Meningitis, Falciparum malaria, Rapid Diagnostic Test, Polymerase Chain Reaction.

INTRODUCTION

Even in endemic countries, malaria might sometime present a diagnostic challenge. At times, malaria RDT as well as microscopy may not yield a positive result leading to a diagnostic dilemma. In the present communication we would try to analyse critically the clinico-pathological events with the goal to find out possible reason(s) of repeated failure to diagnose malaria.

CASE DESCRIPTION

A seven year old boy was admitted to the Ramakrishna Mission Seva Pratisthan Hospital, Kolkata with intermittent fever for seven days accompanied with vomiting and neck rigidity. No complain of headache, convulsion and photophobia was reported. On admission his temperature was 100^{0}F, pulse rate 100/min and BP 100/60. He was conscious but drowsy. Per abdominal examination revealed significant hepatosplenomegaly. WBC count was 9700/cu mm, Hb-10.8 gm/dl and platelet count was 1, 45,000/cu mm. CSF protein was found to be 211 mg/dl with cell count-250 cells/cu mm. Cell types were mainly polymorphonuclear types. There was mild elevation of liver enzymes. Urinalysis revealed no abnormality. CSF as well as blood cultures did not grow any organism even after 72 hours of incubation. He was recommended ceftriaxone followed by Vancomycin. The patient had low intensities of fever for two days just after taking antibiotic. The boy was tested negative for malaria antigen in rapid diagnostic test kit (PfHRP2-detecting RDT) as well as in peripheral blood smear. The child developed high spikes of fever on third day of his antibiotic which persisted for a longer period. His repeat LP showed resolving signs of meningitis with reduced protein 111 mg/dl but the child had persisting fever with hepatosplenomegaly and anaemia. His serum LDH was found to be very high-1138 U/L. On 10thday his Hb started falling and the patient continued to be febrile even after being treated with injection meropenem. The condition of the patient was continuously deteriorating with increased liver enzymes. His repeat LDH was continued to be increasing, 2250 U/L higher than before pointing towards cell lysis. Serum ferritin was very high 2340ng/ml indicative of some infection. Repeat RDT for malaria came negative on 8th day of his hospital admission. In between he was tested negative in direct coomb's test and his entire neurological tests were found to be normal. Finally on day 13th day of his hospital stay the patient came reactive for falciparum malaria in RDT (pLDH specific *Plasmodium falciparum* Genus). Immediately antimalarial ART (artesunate therapy) was started and the patient responded. Subsequently the condition of the patient improved and discharged in a stable condition.

DISCUSSION

In this case falciparum malaria is reported along with bacterial meningitis in a boy of Kolkata, West Bengal, though this type of coincidence has been documented in several parts of the malaria endemic regions of the world [1]. The child was diagnosed with bacterial meningitis at the time of his hospital admission and was put on ceftriaxone followed by vancomycin. Though his meningeal symptoms resolved but fever persisted until antimalarial was started. The most unusual feature in this case is prolonged nonreactive results in RDT and peripheral blood smear study for malaria which led the clinicians to be worried. The question arises here on the origin of malaria-whether the infection was already present which could not be detected earlier or it was a nosocomial infection. The possible explanations for the prolonged delay in malaria antigen detection by microscopy are the following. The boy who tested

negative for malaria in peripheral blood smear might have false negative microscopy due to lack of technical expertise[2]. According to official estimates in India, although about 100 million individuals are investigated for malaria by microscopy every year, fewer than 2% of them are slide-positive[3].

Sequestration, the adherence of infected erythrocytes containing late developmental stages of the parasite (trophozoites and schizonts) to the endothelium of capillaries and venules, which is the characteristic of *Plasmodium falciparum* infections, might be another cause of negative microscopic result[4].The repeated negative results in detection of malaria by RDT might be attributed to the following facts. Firstly- RDT (PfHRP2-detecting RDTs) used for malaria detection can produce negative result due to the deletion of the histidine-rich repeat region of the hrp2 gene of *Plasmodium falciparum* genus [5]. Secondly the boy was admitted in the hospital with seven day's fever, so possibility of being treated with antimalarial drugs prior to his hospital admission could not be ignored. It has been estimated that between 30% and 90% of all patients with acute undifferentiated fever are treated with antimalarial drugs, although only 7–45% of them have laboratory-confirmed malaria[6]. It is well known that the immunosuppressive effect of *Plasmodium falciparum* may predispose to the development of opportunistic infection on its host. In the present case coexistence of bacterial meningitis is reported along with falciparum malaria. The delayed diagnosis of malaria may be influenced by nonspecific cross reaction of natural IgM antibodies with parasite antigen which hinders the malarial antigens to be expressed and hence detected by strip. Low parasite density in this particular case might be another cause of false negativity by RDT. Since most of the RDTs are evaluated by serology based tests, so identification for multiple organisms in a single battery of tests has limitations. Pan microbial microarrays are generally being investigated to facilitate identification of the causative organism when multiple etiological possibilities exist[7]. PCR should be considered a rapid technique for the initial diagnosis of malaria in patients with multiple infections due to its high sensitivity and ability to detect five parasites or less/µl of blood[8]. Hospital induced infection of falciparum malaria might be another cause of delayed diagnosis of the disease which could be justified by the incubation period of *Plasmodium falciparum* in this case.

CONCLUSION

The debate remains unsolved but it becomes evident to adopt alternate techniques like Polymerase Chain Reaction (PCR) for the early detection of malaria to overcome the limitations of RDT in such cases where multiple infections co-exist.

ACKNOWLEDGEMENTS

The contributions of Prof. Dilip Mukherjee, Dr. Suparna Guha, Prof. Amitabha Nandy are greatly acknowledged by the authors.

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